Remarks

Upon entry of the amendment, claims 24-36, 39-43, 46-50, 53-57, and 60-73 will be pending. Claims 1-10, 13-15, and 17-23 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter encompassed by all canceled claims in one or more divisional or continuation applications. Claims 24-26, 30-32, 36, 43, 50, and 57 have been amended to more clearly claim the subject matter Applicants regard as the invention. Support for the amended claims is found throughout the specification as filed. Thus, no new matter has been introduced.

Claims Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 25 and 31 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. *See,* Paper No.15, page 2, second paragraph. More particularly, the Examiner alleges that "[c]onsideration of the specification as filed has revealed that pages 58 and 59 describe SEQ ID NO:73 but not the specific Methionine lacking truncated versions in instant claims 25 and 31." Furthermore, the Examiner asserts that "[c]onsideration of this page 150-151 citation reveals that there is no written disclosure therein of a protein which comprises amino acid residues 2 to 105 of SEQ ID NO: 73." *See*, Paper No. 15, page 2, last paragraph.

Applicants respectfully disagree and traverse.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. The Federal Circuit recently re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed,'" *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). While the applicant must "blaze marks on trees," rather than "simply [provide] the public with a forest of trees," an Applicant is not required to explicitly describe each of the trees in the forest. *See Unocal*, 208 F.3d at 1000. *See also* M.P.E.P. § 2163.02 ("The subject matter of the claim

need not be described literally (*i.e.*, using the same terms or in *haec verba*) in order for the disclosure to satisfy the description requirement."). The Court emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification, rather than whether the specific embodiments had been explicitly described or exemplified. Indeed, as the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Unocal*, 208 F.3d at 1001 (emphasis added).

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one skilled in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *See In re Wertheim*, 541 F.2d 257, 262, 191 U.S.P.Q.2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, Applicants respectfully submit that the Examiner has not met this burden.

Applicants respectfully disagree with the Examiner and submit that one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims in the present application as filed. Applicants further submit that the Examiner has underestimated both the teaching of the present application and the level of skill in the art on the priority date of the present application.

Applicants respectfully point out to the Examiner that claims should be read in light of the specification as a whole. The statement regarding the post-translational modifications of the polypeptides given by Applicants on pages 150-151 applies to all the "polypeptides of the invention," of which SEQ ID NO: 73 is an embodiment. *See*, specification page 150, line 31. The references cited by the Examiner reinforce Applicants' disclosure on page 151, lines 3-6, where it is stated that the modification, including the removal, of the N-terminal Methionine residue depends not only on the host type (eukaryotic or prokaryotic) but also on the residues close to the initial Methionine. The specification envisions several expression systems, both eukaryotic and prokaryotic, *see*, specification page 151, line 7, to page 152, line 27, and the pre- and post-translational modifications naturally occurring in such systems. *See*, specification, page 153, lines 13-28. Therefore, Applicants' statement that "the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells, " envisions polypeptides, produced according to

the teachings of the specification, which may not have a N-terminal Methionine residue. *See*, specification, page 151, lines 1-3.

Thus, one of ordinary skill in the art would conclude that Applicants, at the time of the invention, were in possession of the claimed polypeptides. In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 25, and 31 under 35 U.S.C. § 112, first paragraph.

Claims Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 24-36, 39-43, 46-50, 53-57, and 60-73 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. *See,* Paper No.15, pages 5-6. More specifically, the Examiner states at page 5, second paragraph:

> [S]ince the claimed invention is only supported as to usage regarding a polypeptide consisting only of the entirety of SEQ ID NO: 73, one skilled in the art would not know how to use the claimed invention directed to fragments thereof.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants respectfully point out that claims 36, 43, 50, 57, 64, and 69 contain "consisting of" language. Furthermore, Applicants have amended independent claims 36, 43, 50, and 57 to remove the clause of specificity.

The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the application coupled with information known in the art without undue experimentation. M.P.E.P. § 2164.01(a). Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 443 F.2d 1386, 1390-1391, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been set forth in *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *See id.*

Applicants respectfully submit that the legal standard for evaluating enablement, as cast by the C.C.P.A. and the Federal Circuit, is not whether the specification discloses any or all

alterations that can be made in the claimed proteins that will not alter the functional activity of the proteins, but rather whether proteins encompassed by the claims have at least a single use, and this use can be confirmed, without undue experimentation, by following procedures either described in the specification or otherwise known in the art. *See, In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976):

> To require such a complete disclosure would apparently necessitate a patent with "thousands of examples . . . More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments . . . .

This holding was confirmed by the Federal Circuit. As Judge Rich explained in *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1445 (Fed.Cir. 1991), the statutory enablement requirement is satisfied if the specification "adequately guides the worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility" (emphasis provided). According to M.P.E.P. § 2164.01(b), "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied." *Citing In re Fisher*, 427 F2d 833,839 166 USPQ 18, 24 (CCPA 1970).

Thus, Applicants submit that to be fully enabled, the present specification need only teach the skilled artisan to be able to, for example, use the claimed proteins, or protein fragments, to generate antibodies that immunospecifically bind a protein having the amino acid sequence of SEQ ID NO: 73. Polypeptide fragments are taught in the specification at, *e.g.*, page 99, line 26 to page 100, line 25, and uses for these fragments are also taught in the specification at, *e.g.*, page 101, lines 1-10. Specifically, those fragments can be antigenic (have the ability to bind, or compete with a polypeptide of the invention for binding, to an antibody to the polypeptide of the invention), immunogenic (have the ability to generate antibody which binds to a polypeptide of the invention), have the ability to form multimers with polypeptides of the invention, or have the ability to bind to a receptor or ligand for a polypeptide of the invention. Antibodies can be then generated against those fragments and, in turn, be used to detect the polypeptides of the invention in biological samples. Methods to generate antibodies are described in the specification at, *e.g.*, page 111, line 5 to page 116, line 10, and are well known in the art. Furthermore, methods to use the antibodies generated against fragments of polypeptides of the invention are described in the specification at, *e.g.*, page 128, line 27 to page 133, line 5.

As far as determining whether experimentation is undue, the factors that can be considered have been listed in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *Id. In re Wands* involved an appeal from the Board of Appeals and Patent Interferences, affirming the Examiner's rejection of immunoassay claims on the grounds that making anti-HBsAg antibodies for use in the claimed immunoassay, other than the deposited antibody, would be "unpredictable and unreliable, so that it would require undue experimentation for one skilled in the art to make the antibodies." *Id.* at 1402. Antibodies other than the one deposited were described only in terms of function and only a general method of making and using them was disclosed in the application. *See id.* The facts showed that IgM antibodies were disfavored because they tended to self-aggregate and precipitate, isolating the correct antibodies required screening hundreds of clones, and the appellant's first four attempts were unsuccessful. *See id.* at 1402. Nevertheless, the Federal Circuit found that the disclosure satisfied the requirements under the first paragraph of 35 U.S.C. § 112. The court based its decision on the fact that the invention could be practiced with "readily available starting materials using methods that are well known in the monoclonal antibody art" and because "practitioners of the art are prepared to screen negative hybridomas in order to find one that makes the desired antibody." *See id.* at 1406.

As was the case in *In re Wands*, Applicants have adequately provided the starting materials and guidance to one skilled in the art to make, test, and use the claimed polypeptides. For example, the specification explicitly teaches many structural and functional components of the claimed Secreted Protein HATCM08 such as the full-length polypeptide sequence and the secreted portion of Secreted Protein HATCM08 (*see*, e.g., Table 1, row 23, columns 5 and 11-15; and pages 88-90 of the specification; SEQ ID NO: 33 (the cDNA sequence which encodes the claimed polypeptides); SEQ ID NO: 73 (the full-length polypeptide sequence of Secreted Protein HATCM08)); preferred polypeptide fragments of Secreted Protein HATCM08 (*see, e.g.*, page 57, lines 20-31); antigenic epitopes of Secreted Protein HATCM08 (*see, e.g.*, page 58, line 31 to page 59, line 2; and page 102, line 26 to page 104, line 5); and secondary structural features of the HATCM08 protein including alpha, beta, turn and coil regions, hydrophilicity and hydrophobicity, amphipathic regions, flexible regions, and surface probability (*see, e.g.*, page 100, lines 17-25). These disclosed structural and functional components of the claimed Secreted Protein HATCM08 would be useful, for example, in predicting which amino acid

substitutions would be likely to maintain the structural conformation and electrochemical properties of the protein, which substitutions would likely result in "silent" mutations, and which substitutions would likely affect the antigenicity of the polypeptide. By choosing alterations that maintain or alter certain structures, the desired activity of the claimed protein can be achieved. Importantly, based on these teachings, the skilled artisan would not have to simply rely on trial and error to make and use the invention.

In addition, Applicants respectfully point out that methods were available as of the priority date of the instant application for readily making and identifying numerous altered proteins that retain functions of the original protein (*see*, for example, page 75, lines 4-12 and page 90 lines 18 to page 97, line 31 of the specification).

Applicants submit that it would be routine for one of ordinary skill in the art to make and use an antibody which specifically binds to SEQ ID NO: 73, a fragment of SEQ ID NO: 73, a fusion protein containing SEQ ID NO: 73, or a polypeptide which shares 90% or more sequence identity with SEQ ID NO: 73.

Applicants submit that because of: (1) the availability of routine methods for generating antibodies, (2) the availability of routine techniques for assaying for "specific" antibodies; (3) the knowledge of the amino acid sequence constituting SEQ ID NO: 73; and (4) the high level of skill in the field of immunology and molecular biology, one skilled in the art could routinely generate the claimed antibodies and determine whether these antibodies specifically bind to SEQ ID NO: 73 or variant thereof and satisfy the limitations recited in the claims.

In view of the above discussion, Applicants believe the Examiner's concerns have been fully addressed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 24-36, 39-43, 46-50, 53-57, and 60-73 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

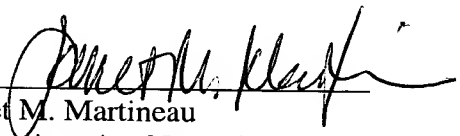
Conclusion

In view of the foregoing remarks, Applicants believe they have fully addressed the Examiner's concerns and that this application is now in condition for allowance. An early notice to that effect is urged. A request is made to the Examiner to call the undersigned at the phone number provided below if any further action by Applicants would expedite allowance of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: April 9, 2003

Respectfully submitted,

By 

Janet M. Martineau
Registration No.: 46,903
HUMAN GENOME SCIENCES, INC.
9410 Key West Avenue
Rockville, Maryland 20850
(301) 315-2723

KKH/JMM/FR/ba

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Ruben et al.

Docket No.: PZ038P1

Application No.: 09/661,453

Group Art Unit: 1631

Filed: September 13, 2000

Examiner: Marschel, A.

For: Secreted Protein HATCM08 (As Amended)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

(Underline indicates text inserted, Strike-through indicates text deleted)

In the Claims:

Claims 24-26, 30-32, 36, 43, 50, and 57 were amended as follows:

24. (Once Amended) An isolated protein ~~comprising~~ **consisting of** amino acid residues ~~24~~ **1** to 105 of SEQ ID NO:73.

25. (Once Amended) The isolated protein of claim 24 which ~~comprises~~ **consists of** amino acid residues 2 to 105 of SEQ ID NO:73.

26. (Once Amended) The isolated protein of claim 24 which ~~comprises~~ **consists of** amino acid residues ~~1~~ **24** to 105 of SEQ ID NO:73.

30. (Once Amended) An isolated protein ~~comprising~~ **consisting of** the amino acid sequence of the ~~secreted portion of the~~ **complete** polypeptide encoded by the HATCM08 cDNA contained in ATCC Deposit No. 203858.

31. (Once Amended) The isolated protein of claim 30 which ~~comprises~~ **consists of** the amino acid sequence of the complete polypeptide encoded by the HATCM08 cDNA contained in ATCC Deposit No. 203858, excepting the N-terminal methionine.

32. (Once Amended) The isolated protein of claim 30 which ~~comprises~~ **consists of** the amino acid sequence of the ~~complete~~ **secreted portion of the** polypeptide encoded by the HATCM08 cDNA contained in ATCC Deposit No. 203858.

36. (Once Amended) An isolated first polypeptide at least 90% identical to a second polypeptide consisting of amino acid residues 24 to 105 of SEQ ID NO:73~~, wherein said first polypeptide is capable of generating or selecting an antibody that specifically binds said second polypeptide~~.

43. (Once Amended) An isolated first polypeptide at least 90% identical to a second polypeptide consisting of the secreted portion of the polypeptide encoded by the HATCM08 cDNA contained in ATCC Deposit No. 203858~~, wherein said first polypeptide is capable of generating or selecting an antibody that specifically binds said second polypeptide~~.

50. (Once Amended) An isolated first polypeptide at least 90% identical to a second polypeptide consisting of amino acid residues 1 to 105 of SEQ ID NO:73~~, wherein said first polypeptide is capable of generating or selecting an antibody that specifically binds said second polypeptide~~.

57. (Once Amended) An isolated first polypeptide at least 90% identical to a second polypeptide consisting of the complete polypeptide encoded by the HATCM08 cDNA contained in ATCC Deposit No. 203858~~, wherein said first polypeptide is capable of generating or selecting an antibody that specifically binds said second polypeptide~~.